Glycine

Type of Posting	Revision Bulletin, Postponement
Posting Date	27–Jul–2018
Official Date	01–Aug–2018
Expert Committee	Non-Botanical Dietary Supplements
Reason for Revision	Compliance

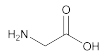
In accordance with the Rules and Procedures of the 2015–2020 Council of Experts, the Non-Botanical Dietary Supplements Expert Committee has postponed the acceptance criteria for monochloroacetic acid and any unspecified impurity, listed in *Table 2* in the test for *Related Compounds* in the Glycine monograph, published in the *First Supplement* to *USP 41–NF 36*.

USP has received comments regarding the implementation of the acceptance criteria for monochloroacetic acid and unspecified impurities. Additional input from stakeholders is required in order to resolve the concerns raised. Interested parties are invited to contact USP for additional information on this topic and to get involved in the dialog on the path forward for these targeted impurities in the Glycine monograph.

The Glycine Revision Bulletin supersedes the monograph becoming official in the *First Supplement to USP 41–NF 36*.

Should you have any questions, please contact Huy Dinh, Senior Scientific Liaison (301-816-8594 or htd@usp.org).

Glycine



$C_2H_5NO_2$ 75.07
Glycine [56-40-6].

DEFINITION

Glycine contains NLT 98.5% and NMT 101.5% of glycine ($C_2H_5NO_2$), calculated on the dried basis.

IDENTIFICATION

• **A. Infrared Absorption ⟨197M⟩**

ASSAY

• **Procedure**

Sample: 150 mg of Glycine
Blank: 100 mL of glacial acetic acid
Titrimetric system
(See *Titrimetry* ⟨541⟩.)
Mode: Direct titration
Titrant: 0.1 N perchloric acid VS
Endpoint detection: Visual
Analysis: Dissolve the *Sample* in 100 mL of glacial acetic acid, and add 1 drop of crystal violet TS. Titrate with the *Titrant* to a green endpoint. Perform the *Blank* determination.
Calculate the percentage of glycine ($C_2H_5NO_2$) in the *Sample* taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample* (mL)
V_B = *Titrant* volume consumed by the *Blank* (mL)
N = actual normality of the *Titrant* (mEq/mL)
F = equivalency factor, 75.07 mg/mEq
W = *Sample* weight (mg)

Acceptance criteria: 98.5%–101.5% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.1%
• **Chloride and Sulfate ⟨221⟩,** *Chloride*
Standard solution: 0.10 mL of 0.020 N hydrochloric acid
Sample: 1 g of Glycine
Acceptance criteria: NMT 0.007%
• **Chloride and Sulfate ⟨221⟩,** *Sulfate*
Standard solution: 0.20 mL of 0.020 N sulfuric acid
Sample: 3 g of Glycine
Acceptance criteria: NMT 0.0065%

Delete the following:

▲• **Heavy Metals,** *Method I* **⟨231⟩:** NMT 20 ppm▲ (Official 1-Jan-2018)

• **Hydrolyzable Substances**
Sample solution: 100 mg/mL of Glycine
Analysis: Boil 10 mL of the *Sample solution* for 1 min, and set aside for 2 h.
Acceptance criteria: The solution appears as clear and as mobile as 10 mL of the same solution that has not been boiled.

Change to read:

▲• **Related Compounds**
Solution A: Transfer 2.16 g of octanesulfonic acid sodium salt to a 1000-mL volumetric flask, add 900 mL of HPLC grade water and 2.0 mL of perchloric acid, and mix to dissolve. Adjust with 5 N sodium hydroxide solution to a pH of 2.2. Dilute with HPLC grade water to volume. Pass the solution through a membrane filter of 0.2-µm pore size.
Solution B: Acetonitrile
Mobile phase: Gradient elution. See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
7	100	0
13	90	10
18	90	10
35	100	0
45	100	0

Standard solution: A mixture of 0.005 mg/mL each of USP Glycine RS, USP Diglycine RS, USP Triglycine RS, and glycine anhydride,[1] and 0.0025 mg/mL of monochloroacetic acid[2] in HPLC grade water. [NOTE—Monochloroacetic acid may be omitted from the *Standard solution* if the article being tested does not contain this substance.]
Sample solution: Transfer 125 mg of Glycine into a 25-mL volumetric flask, dissolve in and dilute with HPLC grade water to volume.
Blank: HPLC grade water
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 200 nm
Column: 4.6-mm × 15-cm; 3-µm packing L1
Column temperature: 25°
Flow rate: 1 mL/min
Injection volume: 20 µL
System suitability
Samples: *Standard solution* and *Blank*
[NOTE—See *Table 2* for the relative retention times.]
Suitability requirements
Interference peaks: Compare the chromatogram obtained from the *Standard solution* with that obtained from the *Blank*. Any peak area from the *Blank* that overlaps or co-elutes with the amino acid peak from the *Standard solution* is NMT 2.0% of that amino acid peak area.
Resolution: NLT 2.0 between the diglycine and triglycine peaks, *Standard solution*
Relative standard deviation: NMT 5.0% each for the specified peaks, *Standard solution*
Analysis
Samples: *Standard solution*, *Sample solution*, and *Blank*
Separately inject the *Blank*, *Standard solution*, and *Sample solution* into the chromatograph. Compare the chromatogram from the *Sample solution* with that from the *Blank*. Disregard any peak observed in both the *Sample solution* and the *Blank*. Identify the amino acid impurities in the *Sample solution* by comparing with those specified in the *Standard solution*.
Separately calculate the percentage of each specified impurity in the portion of Glycine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

[1] Analytical grade with purity NLT 99.0%.
[2] Analytical grade with purity NLT 99.0%.

r_U = peak response of glycine anhydride, monochloroacetic acid, diglycine, or triglycine from the *Sample solution*
r_S = peak response of glycine anhydride, monochloroacetic acid, diglycine, or triglycine from the *Standard solution*
C_S = concentration of glycine anhydride, monochloroacetic acid, USP Diglycine RS, or USP Triglycine RS in the *Standard solution* (mg/mL)
C_U = concentration of Glycine in the *Sample solution* (mg/mL)

Separately calculate the percentage of iminodiacetic acid, hexamethylenetetramine, and any unspecified impurity in the portion of Glycine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of iminodiacetic acid, hexamethylenetetramine, or any unspecified impurity from the *Sample solution*
r_S = peak response of glycine from the *Standard solution*
C_S = concentration of USP Glycine RS in the *Standard solution* (mg/mL)
C_U = concentration of Glycine in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 2*. [NOTE—Disregard any impurity peak less than 0.05%.]

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Glycine anhydride	0.25	0.1
Monochloroacetic acid	0.44	▲[a] ▲ (Postponed on 1-Aug-2018)
Iminodiacetic acid	0.60	0.1
Glycine	1.00	—
Diglycine	1.70	0.1
Triglycine	1.80	0.1
Hexamethylenetetramine	2.47	0.1
Any unspecified impurity	—	▲[b] ▲ (Postponed on 1-Aug-2018)
Total impurities	—	1.0

[a] The limit should be controlled as per International Council for Harmonisation (ICH) M7.
[b] The limit should be based on the maximum daily dose (MDD) of the drug products.

▲ 1S (USP41)

SPECIFIC TESTS

- **LOSS ON DRYING ⟨731⟩**
  Analysis: Dry at 105° for 2 h.
  Acceptance criteria: NMT 0.2%

ADDITIONAL REQUIREMENTS

Change to read:

- **PACKAGING AND STORAGE:** Preserve in well-closed containers ▲at room temperature.▲ 1S (USP41)

Change to read:

- **USP REFERENCE STANDARDS ⟨11⟩**
  ▲USP Diglycine RS▲ 1S (USP41)
  USP Glycine RS
  ▲USP Triglycine RS▲ 1S (USP41)